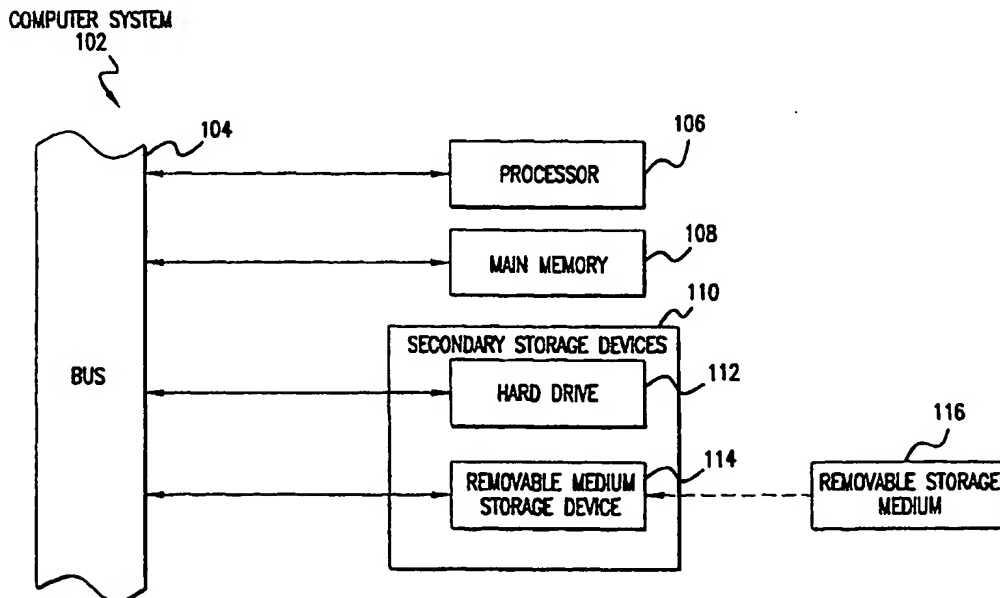




INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁶ : C12N 15/31, C07K 14/315, 16/12, C12Q 1/68		A3	(11) International Publication Number: WO 98/50555
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(21) International Application Number: PCT/US98/08985 (22) International Filing Date: 4 May 1998 (04.05.98) (30) Priority Data: 60/044,031 6 May 1997 (06.05.97) US 60/046,655 16 May 1997 (16.05.97) US 60/066,009 14 November 1997 (14.11.97) US (71) Applicant (for all designated States except US): HUMAN GENOME SCIENCES, INC. [US/US]; 9410 Key West Avenue, Rockville, MD 20850 (US). (72) Inventors; and (75) Inventors/Applicants (for US only): KUNSCH, Charles, A. [US/US]; 4083 Spalding Hollow, Norcross, GA 30092 (US). DILLON, Patrick, J. [US/US]; 1055 Snipe Court, Carlsbad, CA 92009 (US). BARASH, Steven, C. [US/US]; 582 College Parkway #303, Rockville, MD 20850 (US). (74) Agents: BROOKES, A., Anders et al.; Human Genome Sciences, Inc., 9410 Key West Avenue, Rockville, MD 20850 (US).		(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i> (88) Date of publication of the international search report: 14 January 1999 (14.01.99)	

(54) Title: *ENTEROCOCCUS FAECALIS* POLYNUCLEOTIDES AND POLYPEPTIDES

(57) Abstract

The present invention provides polynucleotide sequences of the genome of *Enterococcus faecalis*, polypeptide sequences encoded by the polynucleotide sequences, corresponding polynucleotides and polypeptides, vectors and hosts comprising the polynucleotides, and assays and other uses thereof. The present invention further provides polynucleotide and polypeptide sequence information stored on computer readable media, and computer-based systems and methods which facilitate its use.

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 98/08985

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C12N15/31 C07K14/315 C07K16/12 C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C12N C07K C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 96 33276 A (HUMAN GENOME SCIENCES INC ;UNIV JOHNS HOPKINS (US)) 24 October 1996 see claims 1-7	1-7
A	--- EP 0 756 006 A (INST GENOMIC RESEARCH ;UNIV JOHNS HOPKINS (US); UNIV NORTH CAROLIN) 29 January 1997 see claims 1-5	1-7
A	--- ALTSCHUL S F ET AL: "BASIC LOCAL ALIGNMENT SEARCH TOOL" JOURNAL OF MOLECULAR BIOLOGY, vol. 215, 1990, pages 403-410, XP000604562 cited in the application see the whole document --- -/--	1-7

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents :

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E earlier document but published on or after the international filing date

L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

O document referring to an oral disclosure, use, exhibition or other means

P document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

Z document member of the same patent family

Date of the actual completion of the international search

12 August 1998

Date of mailing of the international search report

17. 11. 1998

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>W.R. PEARSON AND D.J. LIPMAN: "Improved tools for biological sequence comparison" PROC. NATL. ACAD. SCI., vol. 85, April 1988, NATL. ACAD. SCI., WASHINGTON, DC, US; pages 2444-2448, XP002060460 cited in the application see the whole document</p> <p>---</p>	1-7
A	<p>EVERS S & COURVALIN P: "Regulation of VanB-Type vancomycin resistance gene expression by the VanS(B)-VanR (B) two-component regulatory system in Enterococcus faecalis V583." JOURNAL OF BACTERIOLOGY, vol. 178, 1996, pages 1302-1309, XP002073904 see abstract</p> <p>---</p>	1-7
A	<p>CLARK I M ET AL: "ISOLATION AND SEQUENCE DETERMINATION OF AN IMMUNODOMINANT ANTIGEN FROM ENTEROCOCCUS FAECALIS" SERODIAGNOSIS AND IMMUNOTHERAPY IN INFECTIOUS DISEASE, vol. 5, no. 2, July 1993, pages 85-92, XP002050866 see abstract see figure 3</p> <p>---</p>	
A	<p>LOWE A M ET AL: "Cloning of an Enterococcus faecalis endocarditis antigen: homology with adhesins from some oral Streptococci." INFECTION AND IMMUNITY, vol. 63, no. 2, February 1995, pages 703-706, XP002073905 see abstract see figure 2</p> <p>---</p>	1-7
A	<p>BURNIE J P & CLARK I: "Diagnosing endocarditis with the cloned 112 kDa antigen of Enterococcus faecalis." JOURNAL OF IMMUNOLOGICAL METHODS, vol. 123, 1989, pages 217-225, XP002074342 see abstract see page 222, column 1, paragraph 2</p> <p>---</p>	1-7
P,A	<p>XU Y ET AL: "Enterococcus faecalis antigens in human infections." INFECTION AND IMMUNITY, vol. 65, no. 10, October 1997, pages 4207-4215, XP002073906 see abstract</p> <p>-----</p>	1-7

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 98/ 08985

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
See Remark
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-7, see subject 1

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-7

Computer readable medium having recorded thereon the nucleotide sequences depicted in SEQ ID nos. 1-982, a representative fragment thereof or a nucleotide sequence at least 95% identical to a nucleotide sequence depicted in SEQ ID nos. 1-982; a computer-based system for identifying fragments of the *Enterococcus faecalis* genome of commercial importance comprising: a) a data storage means comprising said nucleotide sequence(s); b) search means for comparing a target sequence to the nucleotide sequences of the data storage means of step (a) to identify homologous sequence(s), and c) retrieval means for obtaining said homologous sequence(s) of step (b); a method for identifying commercially important nucleic acid fragments of the *Enterococcus faecalis* genome comprising the step of comparing a database comprising said nucleotide sequence(s) with a target sequence to obtain a nucleic acid molecule comprised of a complementary nucleotide sequence to said target sequence, wherein said target sequence is not randomly selected; a method for identifying an expression modulating fragments of the *Enterococcus faecalis* genome comprising the step of comparing a database comprising said nucleotide sequence(s) with a target sequence to obtain a nucleic acid molecule comprised of a complementary nucleotide sequence to said target sequence, wherein said target sequence comprises sequences known to regulate gene expression;

2. Claims: (8-18) partially

An isolated protein-encoding nucleic acid fragment of the *Enterococcus faecalis* genome, wherein said fragment consists of the nucleotide sequence of any one of the fragments of SEQ ID no.1 depicted in Tables 2 and 3, or a degenerate variant thereof; a vector comprising any one of the fragments of SEQ ID no.1 depicted in Tables 2 and 3; an isolated fragment of the *Enterococcus faecalis* genome, wherein said fragment modulates the expression of an operably linked open reading frame, wherein said fragment consists of the nucleotide sequence from about 10 to 200 bases in length which is 5' to any one of the open reading frames of SEQ ID no.1 depicted in Tables 2 and 3 or a degenerate variant thereof; a method for regulating the expression of a nucleic acid molecule comprising the step of covalently attaching to said nucleic acid molecule a nucleic acid molecule consisting of the nucleotide sequence from about 10 to 100 bases 5' to any one of the open reading frames of SEQ ID no.1 depicted in Tables 2 and 3 or a degenerate variant thereof; an isolated polypeptide encoded by any one of the fragments of SEQ ID no.1 depicted in Table

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

2 and 3; an antibody which selectively binds to any one of said polypeptides, a method for producing a polypeptide in a host cell comprising a) incubating a host containing a heterologous nucleic acid molecule whose nucleotide sequence consists of any one of the fragments of SEQ ID no.1 depicted in Table 2 and 3, under conditions where said heterologous nucleic acid molecule is expressed to produce said protein, and b) isolating said protein;

3-983. Claims: (8-18) partially

Idem as subject 2 but limited to e a c h of the sequences of SEQ ID no. 2 to 982, i.e. invention 3 is limited to the fragments of SEQ ID no. 2 depicted in Tables 2 and 3, invention 4 is limited to the fragments of SEQ ID no. 3 depicted in Tables 2 and 3, and so on.

For the sake of conciseness, the second subject matter is explicitly defined, the other subject matters are defined by analogy hereto.

REMARK:

Although claims 1-4 could, at least partially, be considered as a mere presentation of information, Rule 39.1 (v) PCT, and claims 5-7 at least partially as a program for computers (Rule 39.1(vi) PCT), the search has been carried out as far as possible in our systematic documentation.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 98/08985

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9633276 A	24-10-96	AU 5552396 A	07-11-96
		CA 2218741 A	24-10-96
		EP 0821737 A	04-02-98

EP 0756006 A	29-01-97	CA 2178526 A	08-12-96
		JP 9252787 A	30-09-97
